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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/466,698	06/06/95	SANSONETTI	P 2356.0043-02

HM12/0410
FINNEGAN HENDERSON FARABOW
GARRETT & DUNNER
1300 I STREET NW
WASHINGTON DC 20005-3315

EXAMINER	
NAVARRO, A	
ART UNIT	**PAPER NUMBER**
1645	44

DATE MAILED: 04/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/466,698	Sansonetti et al
Examiner	**Group Art Unit**
Mark Navarro	1645

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *24-46* is/are pending in the application.

Of the above, claim(s) *38* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *24-37 and 39-46* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 24-37 and 39-46, as drawn to methods of modifying the icsA gene of Shigella and Shigella strains comprising an inactivated icsA gene, in Paper No. 45 is acknowledged. The traversal is on the ground(s) that it would not be a serious burden on the Examiner to search the subject matter of the groups of inventions together since the recitation "Shiga-toxin gene" of independent claim 38 (Group II) is also contained in dependent claims of Group I (e.g., claims 26, 30 and 37). This is not found persuasive because each of the inventions is classified in a different class and subclass, which necessitates a separate search. Furthermore, a reference which would anticipate a Shigella strain with an inactivated Shiga-toxin gene would not necessarily anticipate or render obvious a Shigella strain with a modified icsA gene.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 24-37 and 39-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Makino *et al* in view of Mills *et al*, Sekizaki *et al*, Naddif *et al* and Ozenberger *et al*.

The claims are directed to a method for modifying a wild strain of an enteroinvasive Shigella to produce a modified strain of Shigella that can be used for making a vaccine against the wild strain of Shigella comprising inactivating an icsA gene of the wild strain of Shigella, other than only by inactivation by means of a transposon inserted into the gene, so that it is defective in spread within infected cells and from infected to uninfected cells of the host.

First, Applicant's submission filed December 20, 1996 recited Bernardini *et al*. Bernardini *et al* (PNAS Vol. 86, pp 3867-3871, 1989) sets forth that "present evidence indicates that icsA and virG are similar loci." (Page 3871).

Makino *et al* (Cell Vol. 46, pp 551-555, August 1986) teach of a region on the large virulence plasmid of Shigella (virG gene/icsA gene) is required for cell-cell spread and is involved in the pathogenesis of Shigella. Makino *et al* further teaches of transposon insertions into this region, and that the mutant may be a plausible candidate for a vaccine. (See page 554 and abstract).

Makino *et al* does not teach of inactivating the virG/icsA gene by means other then a transposon.

Mills *et al* (Vaccine Vol. 6, pp 116-122, 1988) teach the attenuation of Shigella can be achieved by loss of, or deletion of genes from the large virulence plasmid that specifies bacterial invasion as well as site directed inactivation of the toxin gene. Mills *et al* teaches the potential for reversion to virulence represent possible problems. (See last paragraph).

Sekizaki *et al* (Infection and Immunity Vol. 55(9) pp 2208-2214, 1987) teach of methods of replacing the Shigella toxin gene with a mutant allele. Sekizaki *et al* suggests that toxin production is hazardous.

Ozenberger *et al* (J. Bacteriology Vol. 169 pp 3638-3646, 1987) teaches of using methods of insertion and deletions of the siderophore gene enterobactin to impair the ability to grow.

Nassif *et al* (Infection and Immunity Vol. 55 pp 1963-1969, 1987) teaches of a Shigella flexerni mutant which no longer produces the siderophore aerobactin displays altered extracellular growth capacity. Nassif *et al* teaches that it would not be expected to provide sufficient attenuation, but it would certainly be considered additional security. (See last paragraph).

Given that Makino *et al* have generated Shigella strains with inactivated icsA genes via transposon insertions and that these strains have vaccine potential, and that transposon mutants have the potential for reversion to virulence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have attenuated Shigella by inactivating genes required for bacterial invasion or Shigella toxin as described by Makino *et al* and Sekizaki *et al*, and inactivation of the gene required for aerobactin as taught by Nassif *et al* using methods of allelic exchange and deletion mutagenesis as taught by Mills, Sekizaki *et al*, and Ozenberger *et al* for the expected benefit of developing a vaccine since as described by Sekizaki *et al* toxin production is a hazard in a vaccine.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

April 6, 2001